ABSTRACT

Objective: The goal of this study was to obtain preliminary data on the usefulness of the combination of phentermine and topiramate extended release (phentermine–topiramate) in binge-eating disorder (BED) associated with obesity or overweight. *Design:* Ten participants with BED and obesity or overweightness with at least one weight-related complication received phentermine–topiramate in an open-label, prospective, 12-week trial. The primary outcome measure was change in weight. The study was registered under the identifier NCT02659475 at ClinicalTrials.gov. *Results:* Seven participants completed the study. Phentermine–topiramate treatment was associated with significant reductions in weight, body mass index, binge-eating episode frequency, and measures of global clinical severity, eating disorder psychopathology, and obsessive-compulsive symptoms. Mean daily dose of phentermine–topiramate at endpoint was 6.8 to 41.4mg per day. The most common adverse event (AE) was dysgeusia. There were no serious AEs, and no participants displayed symptoms of medication misuse or withdrawal. *Conclusion:* Phentermine–topiramate could be helpful for weight loss and reduction of binge-eating symptoms in patients with obesity or overweight in addition to BED. Controlled studies are warranted.

Keywords: obesity, binge eating, weight loss, phentermine–topiramate, Qsymia®

ORIGINAL RESEARCH

Combination Phentermine–Topiramate Extended Release for the Treatment of Binge Eating Disorder: An Open-Label, Prospective Study

by ANNA I. GUERDJIKOVA, PHD, LISW; STEPHANIE WILLIAMS, MS; THOMAS J. BLOM, MS; NICOLE MORI, CNP; and SUSAN L. MCELROY, MD

Drs. Guerdjikova and McElroy and Ms. Mori are with the Lindner Center of HOPE in Mason, Ohio, and the Department of Psychiatry and Behavioral Neuroscience at the University of Cincinnati College of Medicine in Cincinnati, Ohio. Mr. Blom is with the Department of Psychiatry and Behavioral Neuroscience at the University of Cincinnati College of Medicine in Cincinnati, Ohio. Ms. Williams is with the Cincinnati Children's Hospital Medical Center in Cincinnati, Ohio.

Innov Clin Neurosci. 2018;15(5–6):17–21

Binge-eating disorder (BED), an eating disorder recognized in the *Diagnostic and Statistical Manual of Mental Disorders*, fifth edition (DSM-5), is characterized by recurrent and distressing episodes of binge eating (eating an unusually large amount of food with a sense of loss of control over eating) without inappropriate compensatory weight-loss behaviors.[1] Known as the most common eating disorder, BED is strongly associated with obesity and obesity-related medical conditions.[2] Treatment targets in BED patients include decreasing binge-eating behavior and, among individuals with overweight or obesity, excessive body weight.

Various treatment strategies, including psychological and pharmacological interventions, aim to reduce binge eating in patients with BED, but not all patients adequately respond to these strategies. Moreover, these treatments are generally either ineffective for weight loss or are associated with problematic adverse events.[3] Lisdexamfetamine dimesylate (LDX), the only medication with regulatory approval for the treatment of BED, is not indicated for weight loss, and its efficacy for the treatment of obesity has not been established.[4] Therefore, well-tolerated novel treatments that reduce both binge-eating behavior and body weight are needed for the management of BED associated with obesity.

The combination of phentermine and topiramate extended-release (phentermine–topiramate, Qsymia®, Vivus, Inc.) is indicated as an adjunct to a reduced-calorie diet and increased physical activity for chronic weight management in adults with a body mass index (BMI) of 30kg/m^2 or greater (obesity) or a BMI

FUNDING: Funding for this study was provided by Lindner Center of HOPE (LCOH).

DISCLOSURES: Vivus Inc. provided the phentermine-topiramate medication for this study. Vivus Inc. had no role in the study design, collection, analysis or interpretation of the data, writing the manuscript, or the decision to submit the paper for publication. Dr.Guerdjikova is employed by the University of Cincinnati College of Medicine and is a consultant for Bracket. Mrs. Mori is employed by the University of Cincinnati College of Medicine and is a consultant for Bracket. Mr. Blom and Mrs.Williams have no conflicts of interest relevant to the content of this article. Dr. McElroy is a consultant to and/or member of the scientific advisory boards of Bracket, F. Hoffmann-La Roche Ltd., MedAvante, Myriad, Naurex, Novo Nordisk, Shire, and Sunovion; is a principal or co-investigator on studies sponsored by the Alkermes, Forest, Marriott Foundation, National Institute of Mental Health, Naurex, Orexigen Therapeutics, Inc., Shire, Sunovion, and Takeda Pharmaceutical Company Ltd.; and is an inventor on United States Patent No. 6,323,236 B2, "Use of Sulfamate Derivatives for Treating Impulse Control Disorders," and along, with the patent's assignee, University of Cincinnati, Cincinnati, Ohio, has received payments from Johnson & Johnson, which has exclusive rights under the patent.

CORRESPONDENCE: Anna I. Guerdjikova, PhD, LISW; Email: anna.guerdjikova@lindnercenter.org

of 25 to 29.9kg/m^2 (overweight) in the presence of at least one weight-related comorbidity, such as hypertension, Type 2 diabetes, or dyslipidemia.[5] Several lines of evidence suggest that phentermine–topiramate would be a useful treatment for individuals with obesity or overweight who also have BED. Several placebo-controlled, randomized trials have shown that topiramate, at doses higher than those used in a phentermine–topiramate combination, is efficacious for reducing binge-eating behavior and body weight in patients with obesity and BED.[6–8] Three other centrally acting weight loss drugs evaluated in the treatment of BED—d-fenfluramine, rimonabant, and sibutramine (which are no longer available because of safety concerns)—have been shown to reduce binge-eating behavior and/or body weight.[9] Our group has observed two patients with BED who experienced the cessation of binge eating and significant weight loss when treated with phentermine–topiramate for a period of three months.[10] In studies of adults with obesity, phentermine-topiramate appeared to be safe and well-tolerated and have low discontinuation rates.[11,12]

To obtain preliminary data on the usefulness of phentermine–topiramate in individuals with BED and either obesity or overweight, we conducted an open-label, prospective, 12-week study of phentermine–topiramate in 10 participants with BED and either obesity or overweight.

METHODS

Study design. This was an open-label, prospective, 12-week, flexible-dose, single-center study conducted at the Lindner Center of HOPE, an affiliate of the University of Cincinnati College of Medicine, in Mason, Ohio. After a one-week screening period, qualified participants entered a 12-week treatment period during which they received open-label phentermine–topiramate. Phentermine–topiramate was discontinued at the last visit of the treatment period. This visit was followed by a one-week post-treatment phone call to assess adverse events.

During the treatment period, study visits were conducted every two weeks. Phentermine–topiramate (phentermine 3.75mg–topiramate 23mg extended-release) was given daily in the morning for 14 days. Thereafter, the dose was increased to phentermine 7.5mg–topiramate 46mg daily and maintained during the treatment period. Following the prescription guidelines, the dose was not further escalated past this point because of the short duration of the trial. Participants were also given nutritional and lifestyle modification counseling following the 2010 Dietary Guidance for Americans (http://www.health.gov/dietaryguidelines/dga2010/DietaryGuidelines2010.pdf) at baseline and their second and fourth visits. Participants were provided with the above link to download the materials or were offered printed copies to take home. At the completion of the study, participants were asked if they planned to continue treatment with phentermine–topiramate, and referrals for further medication management were provided accordingly.

Participant selection criteria. Study participants were recruited using advertisements for a medication trial for people with binge eating and either obesity or overweight. They were eligible for the study if they met the DSM-5 criteria for BED, if they had obesity (defined as a BMI≥30kg/m^2) or overweight (defined as BMI≥27kg/m^2) with at least one weight-related comorbidity, such as hypertension, Type 2 diabetes, or dyslipidemia, and were between 18 and 65 years of age. Participants were excluded if they had a lifetime history of bulimia or anorexia nervosa, a psychotic disorder, or bipolar disorder; had a substance-related or addictive disorder (except a caffeine or tobacco-related disorder) within the six months prior to enrollment; were displaying clinically significant suicidality operationalized as a score ≥2 on Item 9 of the Beck Depression Inventory (BDI)[13] or suicidal ideation on the Columbia-Suicide Severity Rating Scale (C-SSRS);[14] had an unstable medical illness or clinically relevant laboratory results or electrocardiogram (ECG) findings; or required treatment with any drug that might obscure the action of the study medication (e.g., weight-loss drugs, psychostimulants, wakefulness-promoting agents, drugs with serotonergic properties, antidepressants, and antipsychotics). Women were excluded if they were pregnant, lactating, or, if fertile, not practicing a medically accepted form of contraception.

Participant evaluation. The Institutional Review Board at the University of Cincinnati College of Medicine approved the study protocol. All participants provided written informed consent before the administration of any study procedures. Participants were enrolled in the study, which was registered under the identifier NCT02659475 at the ClinicalTrials.gov portal, from September 3, 2015, to April 13, 2016. The study was conducted at the Lindner Center of HOPE in Mason, Ohio, in full compliance with the United States Food and Drug Administration (FDA) Guidelines for Good Clinical Practice and the Declaration of Helsinki.

All participants underwent a screening evaluation that included the Structured Clinical Interview for DSM-IV-TR (SCID-I/P)[15] to establish the diagnosis of BED and determine comorbid Axis I diagnoses; the Eating Disorder Examination Questionnaire (EDE-Q)[16] to confirm the diagnosis of BED and establish binge-eating episode frequency; the BDI[13] to assess depressive symptoms; the C-SSRS[14] to assess lifetime suicidality; a medical history and physical examination; vital signs; height and weight measurements to determine BMI; ECG; urine pregnancy and toxicology tests; and blood chemical and hematological tests. Of note, the DSM-IV-TR SCID can be used to assess DSM-5 BED with one minor change in the question regarding the frequency and duration of binge-eating behavior (i.e., binge eating occurs, on average, at least once a week for 3 months per DSM-5, rather than 2 days a week for 6 months per the DSM-IV-TR).

Outcome measures. The primary outcome measure was the change in weight from baseline to Week 12/early termination (ET). Secondary outcome measures included BMI, binge eating episode frequency (number of binge eating episodes in the last seven days assessed with the EDE-Q), and scores on the Clinician Global Impression Severity (CGI-S) scale,[17] Yale-Brown Obsessive Compulsive Scale Modified for Binge Eating (YBOCS-BE),[18] Binge Eating Scale (BES),[19] EDE-Q eating psychopathology scales, and BDI. Other outcome assessments included cessation of binge eating (the absence of binge eating episodes for four consecutive weeks); systolic and diastolic blood pressure; and measures of metabolic variables (e.g., fasting glucose, A1C, and lipid profile). Safety measurements conducted at each visit were vital signs, suicidality, and adverse events. A physical examination, routine laboratory evaluations (including hematology, serum chemistry, and urinalysis), and ECG were performed at the initial screening and at the study's end. Urine pregnancy test was performed monthly. Participants were to be discontinued if they displayed clinically significant suicidality (a score ≥2 on Item 9 of the BDI, a C-SSRS-defined suicidal ideation, or

TABLE 1. Clinical characteristics and measures, by participant

ENROLLMENT (N)	AGE/ DURATION OF ILLNESS (YEARS)	RACE/SEX	BASELINE WEEKLY BINGE-EATING EPISODE FREQUENCY	BASELINE WEIGHT (KG)/ BMI	WEEKS OF TRIAL COMPLETED	WEEKLY BINGE-EATING EPISODE FREQUENCY AT STUDY'S END	WEIGHT (KG)/ BMI AT STUDY'S END	CHANGE IN WEIGHT (KG)	OPTED TO CONTINUE TREATMENT WITH STUDY DRUG
1	41/29	W/F	2.25	110.7/36.4	12	0	98.9/32.5	-11.8	No
2	51/31	W/F	2.5	101.2/38.2	12	0	99.6/37.6	-1.6	No
3	28/5	W/F	3.0	113.7/39.2	12	0.25	112.4/38.7	-1.3	No
4	33/25	W/F	2.0	85.4/29.4	12	0	75.3/25.9	-10.1	Yes
5	53/8	W/M	0.5	150/47.4	12	0	142.6/45.4	-7.4	Yes
6	39/22	W/F	0.75	101.8/36.3	12	0.25	99/35.3	-2.8	No
7	51/31	W/F	4.0	99.5/36.8	12	0.5	95.6/35.3	-3.9	Yes
8	57/50	W/F	10.0	98.4/33.8	4	3.75	97.3/33.5	-1.1	No data
9	47/42	W/F	7.5	103.5/37.7	10	3	102.3/37.5	-1.2	No data
10	53/41	W/F	2.0	127.1/41.9	2	No data	128/42.2	+0.9	No data

AE: adverse event; BMI: body mass index; BED: binge-eating disorder; F: female; ICF: information consent form; n: number; W: white
Subject 1 achieved remission in BED (8 weeks with no binge episodes); she reported she would consider restarting phentermine-topiramate if BED reoccurred.
Subject 2 achieved remission in BED (6 weeks with no binge episodes); she reported she would consider various treatment options if BED reoccurred.
Subject 3 opted to not continue phentermine-topiramate, as she was not satisfied with her weight loss.
Subject 6 opted to not continue phentermine-topiramate because of the cost associated with taking the medication.
Subject 8 withdrew ICF, as she did not feel her BED approved enough to continue on the medication.
Subject 9 was lost to follow-up.
Subject 10 stopped the medication because of AE (i.e., dizziness, which completely resolved upon study medication discontinuation).

a C-SSRS-defined suicide attempt). Adherence with dosing requirements was monitored using a returned pill count.

Statistical methods. The statistical methods employed were similar to those used in previous open-label BED pharmacotherapy trials.[20,21] The primary efficacy analyses used longitudinal mixed models, which examined the change of each outcome during the treatment period. These analyses were conducted on the intent-to-treat (ITT) population (i.e., all participants who took 1 dose of study medication) and used all data from these participants. Time was included as the only independent variable and was modeled as a continuous variable in weeks, except for some outcomes, where time was expressed as the square root of days, since study drug initiation was used to produce a more linear relationship with the outcome. For the binge-eating episode frequency outcome, a logarithmic transformation (log [binges/week + 1]) was used to stabilize the variance and normalize the data. To account for the correlation resulting from repeated measures, the MIXED procedure (SAS Institute, Cary, North Carolina, USA) was used. These mixed models allowed for random coefficients for the intercept and time variable, and/or a correlated error structure. The corrected Akaike information criterion was used to select the best-fitting model.

Secondary analyses were performed using the last observation carried forward for each outcome. One-sample t-tests (or Wilcoxon rank-sum tests for non-normal data) were used on the baseline-to-endpoint change scores to test for significant changes from baseline.

The safety population consisted of all participants who received at least one dose of study medication. Adverse events were tabulated for descriptive purposes. Changes in laboratory measures were examined using one-sample t-tests (or Wilcoxon rank-sum tests for non-

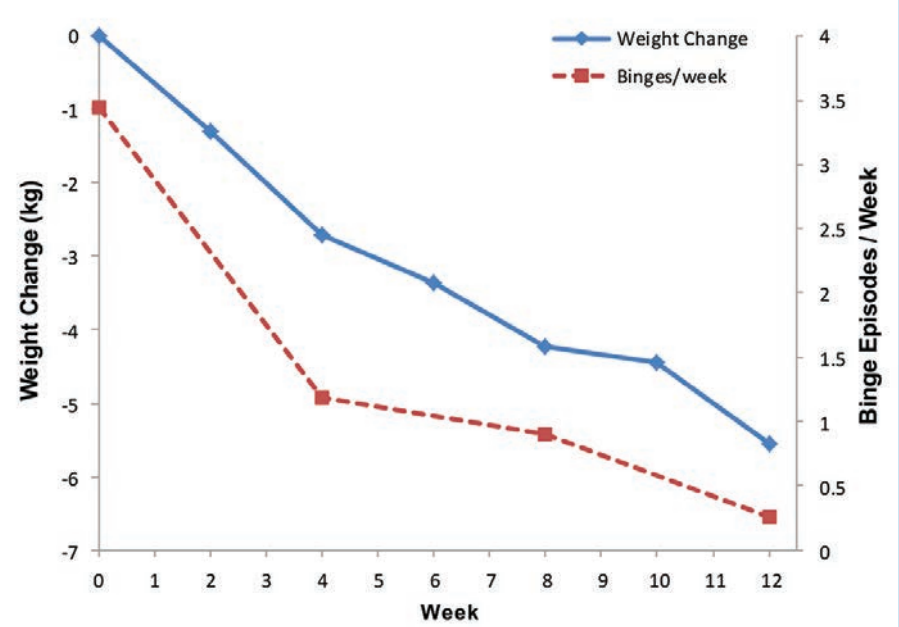

FIGURE 1. Cumulative mean weight (kg) change and weekly binge episodes over 12 weeks of phentermine–topiramate treatment

TABLE 2. Outcome measures before and after treatment with phentermine-topiramate and analysis of change in outcome

OUTCOME MEASURE	MEAN (STANDARD DEVIATION)			MEAN (95% CI) CHANGE FROM BASELINE				
	BASELINE (N=10)	ENDPOINT (N=10)	WEEK 12 (N=7)	LONGITUDINAL ANALYSIS CHANGE AT WEEK 12	P-VALUE	ENDPOINT ANALYSIS CHANGE AT ENDPOINT	*P*-VALUE	EFFECT[b] SIZE
Weight (kg)	109.1 (18.1)	105.1 (18.7)	103.3 (20.5)	-4.9 (-7.2, -2.5)	<0.01	-4.0 (-7.1, -1.0)	0.02	0.22
BMI (kg/m^2)	37.7 (4.8)	36.4 (5.4)	35.8 (5.9)	-1.6 (-2.4, -0.8)	<0.01	-1.3 (-2.3, -0.3)	0.02	0.27
Binge episodes per week	3.4 (3.0)	0.9 (1.4)	0.2 (0.3)	0.06 (0.02, 0.24)[a]	<0.01	-2.7 (-4.1, -1.2)	<0.01	0.90
CGI-S	4.4 (0.8)	2.3 (1.3)	1.6 (0.5)	-2.8 (-3.5, -2.0)	<0.01	-2.1 (-2.8, -1.4)	<0.01	2.63
YBOCS-BE obsessions	10.4 (3.1)	2.1 (1.5)	2.1 (1.9)	-8.6 (-10.8, -6.4)	<0.01	-8.3 (-10.3, -6.3)	<0.01	2.68
YBOCS-BE compulsions	9.7 (1.8)	2.2 (3.3)	1.1 (1.9)	-8.9 (-10.9, -6.9)	<0.01	-7.5 (-10.1, -4.9)	<0.01	4.17
YBOCS-BE total	20.1 (4.7)	4.3 (3.9)	3.3 (3.3)	-17.6 (-21.3, -13.9)	<0.01	-15.8 (-19.3, -12.3)	<0.01	3.36
BES	46.1 (5.9)	31.9 (12.0)	30.0 (8.8)	-16.3 (-26.5, -6.0)	<0.01	-14.2 (-23.4, -5.0)	<0.01	2.41
EDE-Q restraint	2.3 (1.9)	2.4 (1.4)	2.5 (1.1)	0.1 (-0.9, 1.2)	0.78	0.4 (-0.8, 1.6)	0.48	-0.21
EDE-Q eating concern	1.9 (1.5)	1.3 (1.5)	0.6 (0.6)	-0.9 (-1.7, -0.1)	0.03	-0.6 (-1.5, 0.3)	0.15	0.40
EDE-Q shape concern	2.6 (1.0)	1.8 (0.7)	1.8 (0.8)	-0.6 (-1.2, 0.0)	0.05	-0.6 (-1.1, -0.1)	0.03	0.60
EDE-Q weight concern	2.7 (1.3)	1.6 (0.7)	1.5 (0.7)	-1.2 (-1.9, -0.6)	<0.01	-1.1 (-1.9, -0.2)	0.02	0.85
EDE-Q total	2.4 (1.0)	1.8 (0.6)	1.6 (0.4)	-0.8 (-1.4, -0.1)	0.03	-0.5 (-1.0, 0.1)	0.07	0.50
BDI	6.2 (3.5)	4.7 (3.6)	5.1 (3.6)	-2.8 (-5.3, -0.4)	0.03	-1.9 (-4.0, 0.3)	0.08	0.54

CI: Confidence interval; n: number; BMI: body mass index (weight in kg divided by height in m^2); CGI-S: Clinical Global Impression-Severity; YBOCS-BE: Yale-Brown Obsessive-Compulsive Scale Modified for Binge Eating; BES: Binge Eating Scale; EDE-Q: Eating Disorder Examination Questionnaire; BDI: Beck Depression Inventory; CI, confidence interval

[a]Log transformation used; estimate equals Week 12 divided by Week 0

[b]Effect size=change from BL to endpoint/BI standard deviation; + numbers indicate reduction

normal data). All statistical analyses were two-sided, with a significance level of 0.05, and were conducted using SAS version 9.4 (SAS Institute, Cary, North Carolina, USA).

RESULTS

Of 11 individuals screened, 10 were enrolled and received at least one dose of phentermine-topiramate (Table 1). Nine participants were female; their mean (standard deviation [SD]) age at baseline was 45.3 (9.6) years; all were white; their mean BMI (SD) was 37.7 (4.8)kg/m^2; and the mean age of BED (SD) onset was 16.9 (11.6) years. Nine participants had obesity, and one had overweight with comorbid dyslipidemia. Seven participants completed the 12-week trial; the remaining three discontinued prematurely after a mean (SD) of 41.3 (29.5) days in the study for the following reasons: consent withdrawn (n=1), adverse event (n=1), and lost to follow-up (n=1). At endpoint, the mean (SD) daily dose of phentermine–topiramate was 6.8 (1.6)mg–41.4 (9.7)mg, and the median daily dose was phentermine 7.5mg–topiramate 46mg. For the seven participants who completed the trial, the mean daily dose at Week 12 was phentermine 7.5mg–topiramate 46mg.

The observed mean values for the outcome measures at Week 12 or last observation, along with the analysis of change in outcome measures, are presented in Table 2. Participants displayed a mean (standard error) weight reduction of 4.9 (1.2)kg in the primary longitudinal analysis (p<0.01). Mean body weight decreased steadily from baseline to the study endpoint (Figure 1). Significant reductions were also seen in BMI, binge-eating episode frequency, and scores on the CGI-S, YBOCS-BE, BES, EDE-Q, and BDI. A similar pattern was observed in the secondary baseline to endpoint analyses. Four participants had cessation of binge eating at study termination, and two of these lost at least five percent of their baseline weight at endpoint. Weekly binge-eating episode frequency steadily decreased from baseline to endpoint but was not significantly correlated with weight change.

The most common adverse events reported by participants were dysgeusia (n=3), constipation (n=2), dry mouth (n=2), and tiredness (n=2) (Table 3). The one participant who withdrew because of an adverse event experienced dizziness, which completely resolved upon study medication discontinuation. There were no serious adverse events and no statistically significant changes in vital signs. Three laboratory tests had significant changes from baseline to Week 12: potassium decreased, with a mean (SD) change = -0.4 (0.2), p<0.01; chloride increased, with a mean (SD) change = 2.7 (2.3), p=0.04; and total bilirubin increased, with a mean (SD) change = 0.09 (0.07), p=0.02. No participant had a clinically significant change in any of these parameters. Also, no participant displayed symptoms of medication misuse or withdrawal.

TABLE 3. Adverse events

DESCRIPTION	PARTICIPANTS WITH EVENT
Dysgeusia	3 (30%)
Constipation	2 (20%)
Dry mouth	2 (20%)
Tiredness	2 (20%)
Dizziness	1 (10%)
Dysphoria	1 (10%)
Headache	1 (10%)
Headache - caffeine withdraw	1 (10%)
Increased allergy symptoms	1 (10%)
Increased thirst	1 (10%)
Insomnia	1 (10%)
Jittery	1 (10%)
Rash	1 (10%)
Rosacea exacerbation	1 (10%)
Sciatic nerve pain exacerbation	1 (10%)
Shoulder pain exacerbation	1 (10%)
Stomach ache	1 (10%)

DISCUSSION

Twelve weeks of open-label treatment with phentermine–topiramate in combination with dietary counseling in 10 individuals with BED and either obesity or overweight was associated with significant reductions in body weight, BMI, binge-eating episode frequency, global illness severity, obsessive-compulsive features of binge eating, and BED psychopathology.

Of note, the median daily dose of topiramate (46mg) used in this study was at least four times lower than that used in studies of topiramate monotherapy in BED, where the median doses were between 212 and 300mg.[6,7] Some patients with BED who are unable to tolerate higher doses of topiramate alone might benefit from lower doses of topiramate in combination with phentermine.

The observed significant laboratory changes were within healthy reference ranges and were not associated with clinical symptoms. However, decreased serum potassium values (defined as <3.5mEq/L at two consecutive visits or at the final visit) are described in the phentermine–topiramate prescribing information[5] and need to be further evaluated in patients with BED and either obesity or overweight receiving the compound.

Limitations. Several notable limitations of this study should be considered. First, and most important, because the study was uncontrolled, the observed improvement could represent a response to dietary therapy, a placebo response, or rater and/or participant bias. Indeed, behavioral weight loss therapy has been associated with improvement of both binge eating and body weight in patients with BED.[22] Regarding placebo response, binge eating has been associated with a substantial response to the placebo in many randomized, controlled trials.[23] However, the placebo is not associated with weight loss in BED, and the weight loss seen in this trial suggests phentermine–topiramate could be associated with real therapeutic effects. Another limitation is that the study group was small and mostly female and many forms of psychiatric and medical pathology were excluded. Additionally, treatment duration was short, which did not allow for titration of study medication to the maximum allowed phentermine–topiramate daily dose of 15 to 92mg. It is possible that effects on body weight loss and binge eating could be optimized with longer treatment duration and use of higher doses. Finally, the results might not generalize to larger, more diverse groups of individuals with BED or to longer treatment periods. The use of phentermine–topiramate in BED must therefore be considered experimental at this time.

CONCLUSION

In summary, in an open-label, prospective, 12-week, flexible-dose trial, phentermine–topiramate appeared to be effective and well-tolerated for reducing body weight, BMI, and binge eating symptomatology in individuals with BED and either obesity or overweight. Because of the study's limitations, these results should be considered highly preliminary. Nonetheless, they suggest that adequately sized randomized, placebo-controlled trials of phentermine–topiramate in individuals with BED and either obesity or overweight should be conducted.

CONTRIBUTORS

Drs. Guerdjikova and McElroy designed the study and wrote the protocol. Dr. Guerdjikova, N. Mori, and S.Williams assessed participants throughout the study. Mr. Blom conducted the statistical analysis. Dr. Guerdjikova wrote the first draft of the manuscript, and all authors contributed to and have approved the final manuscript.

REFERENCES

1. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders.* 5th ed. Washington, DC: American Psychiatric Association; 2013.
2. Kessler RC, Berglund PA, Chiu WT, et al. The prevalence and correlates of binge eating disorder in the World Health Organization World Mental Health Surveys. *Biol Psychiatry.* 2013; 73(9):904–914.
3. Mcelroy SL, Guerdjikova AI, Mori N, et al. Overview of the treatment of binge eating disorder. *CNS Spectr.* 2015;20(6):546–556.
4. United States Food and Drug Administration. Vyvanse Drug Approval Package. Available at: https://www.accessdata.fda.gov/darugsatfda_docs/nda/2007/021977s000TOC.cfm. Accessed February 12, 2015.
5. United States Food and Drug Administration. Highlights of prescribing information, Qsymia (phentermine and topiramate extended release). Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2012/022580s000lbl.pdf. Accessed: June 20, 2018.
6. Mcelroy SL, Arnold LM, Shapira NA, et al. Topiramate in the treatment of binge eating disorder associated with obesity: a randomized, placebo-controlled trial. *Am J Psychiatry.* 2003;160(2):255–261.
7. Mcelroy SL, Hudson JI, Capece JA, et al. Topiramate for the treatment of binge eating disorder associated with obesity: a placebo-controlled study. *Biol Psychiatry.* 2007;61(9):1039–1048.
8. Claudino AM, De Oliveira IR, Appolinario JC, et al. Double-blind, randomized, placebo-controlled trial of topiramate plus cognitive-behavior therapy in binge-eating disorder. *J Clin Psychiatry.* 2007;68(9):1324–1332.
9. Cheung BM, Cheung TT, Samaranayake NR. Safety of antiobesity drugs. *Ther Adv Drug Saf.* 2013;4(4):171–181.
10. Guerdjikova AI, Fitch A, Mcelroy SL. Successful treatment of binge eating disorder with combination phentermine/topiramate extended release. *Prim Care Companion CNS Disord.* 2015;17(2).
11. Alfaris N, Minnick AM, Hopkins CM, et al. Combination phentermine and topiramate extended release in the management of obesity. *Expert Opin Pharmacother.* 2015;16(8):1263–1274.
12. Khera R, Murad MH, Chandar AK, et al. Association of pharmacological treatments for obesity with weight loss and adverse events: a systematic review and meta-analysis. *JAMA.* 2016;315(22):2424–2434.
13. Beck AT, Ward CH, Mendelson M, et al. An inventory for measuring depression. *Arch Gen Psychiatry.* 1961;4:561–571.
14. Posner K, Oquendo MA, Gould M, et al. Columbia Classification Algorithm of Suicide Assessment (C-CASA): classification of suicidal events in the FDA's pediatric suicidal risk analysis of antidepressants. *Am J Psychiatry.* 2007;164(7):1035–1043.
15. First MB, Spitzer RL, Gibbon M, Williams JBW. Structured clinical interview for DSM-IV-TR Axis I disorders, research version, patient edition. (SCID-I/P) New York, NY: Biometrics Research, New York State Psychiatric Institute; 2002.
16. Fairburn CG, Beglin SJ. Assessment of eating disorders: interview or self-report questionnaire? *Int J Eat Disord.* 1994;16(4):363–370.
17. Guy W. ECDEU Assessment Manual for Psychopharmacology. Rockville, MD: National Institute of Mental Health; 1976.
18. Deal LS, Wirth RJ, Gasior M, et al. Validation of the Yale-Brown Obsessive Compulsive Scale modified for binge eating. *Int J Eat Disord.* 2015;48(7):994–1004.
19. Gormally J, Black S, Daston S, Rardin D. The assessment of binge eating severity among obese persons. *Addict Behav.* 1982;7(1):47–55.
20. Mcelroy SL, Guerdjikova AI, Winstanley EL, et al. Sodium oxybate in the treatment of binge eating disorder: an open-label, prospective study. *Int J Eat Disord.* 2011;44(3):262–268.
21. Mcelroy SL, Kotwal R, Hudson JI , et al. Zonisamide in the treatment of binge-eating disorder: an open-label, prospective trial. *J Clin Psychiatry.* 2004;65(1):50–56.
22. Grilo CM, Masheb RM, Wilson GT, et al. Cognitive-behavioral therapy, behavioral weight loss, and sequential treatment for obese patients with binge-eating disorder: a randomized controlled trial. *J Consult Clin Psychol.* 2011;79(5):675–685.
23. Jacobs-Pilipski MJ, Wilfley DE, Crow SJ, et al. Placebo response in binge eating disorder. *Int J Eat Disord.* 2007;40(3):204–211. ICNS